Feasibility of Concurrent Cisplatin and Extended Field Radiation Therapy Using IMRT for Carcinoma of the Cervix

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Purpose: The orderly nodal pattern of spread of cervical cancer has generated interest in prophylactic paraaortic irradiation. An RTOG prospective randomized trial of extended field (EFRT) versus pelvic RT demonstrated an improved survival in the EFRT arm at the cost of increased acute and late toxicity. A subsequent RTOG study demonstrated improved survival in patients receiving pelvic RT and concurrent chemotherapy compared to EFRT alone with no excessive toxicity or treatment prolongation. The RTOG experience with EFRT delivered on a BID schedule with concurrent chemotherapy for carcinoma of the cervix has been associated with unacceptably high acute morbidity (31% grade 4). A GOG study using a different fractionation and chemotherapy schedule was associated with acceptable acute toxicity but resulted in a more protracted treatment course. Currently, the RTOG is investigating EFRT with cisplatin and amifostine as a strategy to decrease toxicity. This institution evaluated the feasibility of weekly cisplatin concurrent with EFRT using an intensity modulated radiotherapy (IMRT) technique to decrease acute toxicity.

Methods: All patients receiving definitive treatment for cervical cancer were treated with EFRT using IMRT technique (5 angles). Patients were planned with either a contrasted CT or PET CT scan without respiratory gating. Vac bag immobilization was used around thighs/legs. Gold marker seeds were placed in the cervix and lower extent of vaginal extension. A vaginal CT marker was placed at the top of planning scan. The treatment volume included the pelvic paraaortic, iliac, and paraaortic nodes to the top of L1. The primary focus of the study was on the pelvic and 2 with both pelvic and paraaortic nodes. An additional patient had pelvic nodal disease detected at the time of nodal sampling. All patients completed the prescribed course of EFRT. Median treatment length was 39 days (range 36-53). Treatment breaks of 2 and 3 days were required due to bone marrow toxicity in 2 patients. The final week of EFRT was delivered only in 2 patients because of neutropenia. No patient attained Grade 3 or 4 GI or GU toxicity. Mean nadir ANC and platelet counts were 2019 (range 620-3,250) and 153,000 (range 39, 000- 369,000), respectively. Toxicity is summarized in the table.

Conclusion: In this prospective clinical study, IMRT technique was used to successfully deliver EFRT with concurrent chemosensitization. The technique was associated with an acceptable acute toxicity without significant treatment prolongation. The hematological toxicity generally occurred at the end of the treatment course and did not interrupt therapy in most cases. The incidence of grade 3 hematologic toxicity was similar to the reported toxicity in the GOG study of EFRT and chemotherapy as well as the RTOG pelvic RT and concurrent chemotherapy arm. This new role for IMRT merits further evaluation with larger patient numbers and longer follow-up. The impact of simultaneous nodal boost using PET-CT planning will need to be assessed in terms of late toxicity and disease control.

Transverse, Frontal and Sagittal Image

Dose Volume Histogram

![Image](Transverse, Frontal and Sagittal Image)

Toxicity

<table>
<thead>
<tr>
<th>GI</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>36.1%</td>
<td>2</td>
<td>9.5%</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>23.8%</td>
<td>2</td>
<td>9.5%</td>
<td>0</td>
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<tr>
<td>Skin</td>
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<td>4.8%</td>
<td>2</td>
<td>9.5%</td>
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<tr>
<td>6</td>
<td>28.6%</td>
<td>3</td>
<td>14.3%</td>
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Prophylactic PAN RT
- RTOG 79-20 prospective randomized trial of extended field RT vs pelvic RT showed an improved survival in the extended field arm
- RTOG 90-01 prospective randomization between extended field RT vs pelvic RT plus cisplatin and fluorouracil. Significantly improved survival shown in chemo arm with no increase in toxicity

Extended Field RT and Concurrent Chemotherapy
- Phase II trials done by RTOG and GOG assessing EFRT with cisplatin and FU in patients with known PAN disease
- RTOG 92-10 used bid schedule (1.2 Gy to 48 Gy) with boost to 54-58 Gy. Excessive acute and late toxicity encountered:
  - Acute: 31% Grade 4 and 1 Grade 5
  - Late: 17%, Mostly Grade 1
- GOG 125 used slightly lower dose cisplatin (50 mg/m² in RTOG) and daily rather than BID RT (45 Gy in 1.5 Gy fractions)
- Acute toxicity felt to be acceptable (Grade 3 / 4 GI toxicity in 6% and 15% in Grade 3 / 4 GU toxicity)
- 14% Late complications, majority in the pelvis (proctitis)